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Types and Frequencies of Pathologies in Endometrial Curettings of Abnormal Uterine Bleeding

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Introduction: Abnormal uterine bleeding is one of the most frequently encountered and perplexing condition in adult women. Its causes include a wide spectrum of diseases. An important diagnostic method is endometrial curettage. It provides information regarding specific and nonspecific infections and malignancy. Histological evaluation can also highlight the incidental findings of organic causes as polyps or malignancy in cases in which no organic cause of bleeding was initially suspected.

Objective: The objectives of the study were to determine the types and frequencies of pathologies in endometrial curettings of abnormal uterine bleeding & compare different endometrial pathologies in patient groups made according to age, presenting complaints and parity.

Study Design: It was a comparative study.

Setting: Histopathology department, Pakistan institute of Medical Sciences (PIMS), Islamabad.

Material and Methods: H&E slides of endometrial curretings of 25 patients were evaluated. Diagnosis was made by correlating the morphological findings with the clinical history over a period of one year i-e 14th Oct. 2004 to 14th Oct. 2005

Results: The most common complaint was polymennorhagia 36% (18/50) followed by mennorhagia 30% (15/50). There were two cases of oligomennorhoea (2%) and five cases of post menopausal bleeding (10%). Frequencies of endometrial pathologies was Estrogen dominanance pattern 42% (21), Anovulatory endometrium and chronic endometritis 24% (12) each, atrophic endometrium and endometrial carcinoma 2% (1) each and 6% (3) cases of pill effect endometrium.

Conclusion: Our study on endometrial curettings in abnormal uterine bleeding revealed clustering of cases around perimenopausal age. There was relative estrogen excess termed as Estrogen Dominance Pattern (EDP) over Progesterone leading to specific changes such as clusters of thickened blood vessels, spindly stroma, weak or absent secretory changes in the glands and stroma with or without polyp formation. We also noted frequent anovulatory pattern in the old age.

Key words: Frequency, Endometrial curettings, Abnormal uterine bleeding.

Introduction

Abnormal uterine bleeding is one of the most frequently encountered and perplexing condition in adult women.[1] Its causes include a wide spectrum of diseases that may be subdivided into reproductive tract diseases, iatrogenic causes and systemic diseases.[2] Chronic unopposed estrogenic stimulation of the endometrial lining, which is an important cause of abnormal uterine bleeding, increases the risk of both endometrial hyperplasia and endometrial carcinoma. Many women with abnormal uterine bleeding may undergo unwarranted hysterectomy without a definite diagnosis.[3]

Dilatation and curettage is a useful and cost effective method of detecting intrauterine pathologies and very few lesions escape detection[4, 5] It clearly shows the hormonal response of endometrium and provides useful information regarding atrophy, specific and non-specific infections, polyps and/or malignancy.[6] Our study is aimed at determining the types and frequencies of endometrial pathologies in cases of abnormal uterine bleeding in reference to different patient groups, parity and clinical symptomatology. This may be of help in planning the therapeutic strategies by the gynecologists.

Materials and Methods

A total of fifty cases of endometrial curettings with a history of dysfunctional uterine bleeding were selected from Maternal and Child Health Center (MCH). The specimens were processed in the

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The study spanned from 14th Oct. 2004 to 14th Oct. 2005. It was a comparative study based on convenience (non-probability) sampling. Data were collected according to proforma. Relevant history and biopsy were supplied by the MCH centre PIMS. Ultrasound examination had been done, the endometrial curettings were received in 10% formalin and gross descriptive details like color, weight etc. were noted. Approximately 3 mm. thick sections were taken. slides were stained by routine hematoxylin and eosin stains. The trainee and the supervisor made the final diagnosis after correlating histopathological findings with the clinical data.

All women undergoing curettage for the reason of abnormal uterine bleeding were included while those with systemic or pelvic causes of bleeding, without adequate history, without adequate samples and unfixed specimen were excluded.

All data were entered into SPSS version 10. Frequencies of various pathologies like hyperplasia, hormonal imbalance, endometritis, malignancy etc. were calculated. Chi square test was used to compare the different pathologies among the said patient groups.

Results

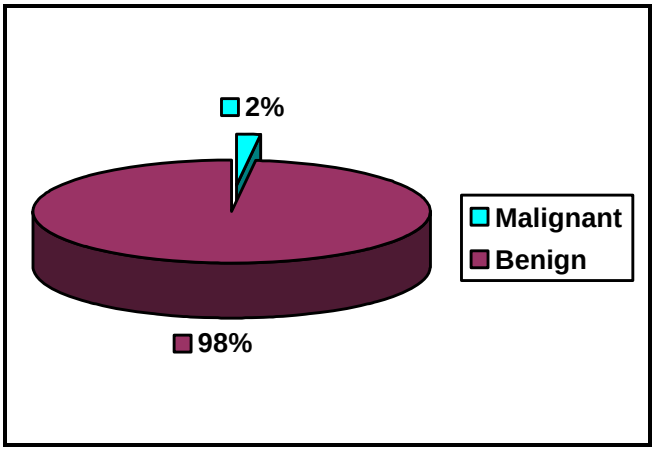
A total of 416 curettage specimens were submitted for histopathological examination during the study period. Out of 416 cases, 50 samples were selected which fulfilled the inclusion criteria for the study. Twenty four patients had undergone hysteroscopic examination in addition to conventional dilatation & curettage. Also ultrasound examination had been done in all cases. Specimen were received as multiple soft tissue fragments ranging in weight from 0.5g to 2g. The frequencies of various types of endometrial pathologies observed are given in the Table I.

Among 50 cases of endometrial curettage only one case had malignancy i.e. endometroid adenocrcinoma (Figure 2) while in the rest there was either hormonal imbalance (55%) or infection (24%). Estrogen dominance pattern of the endometrium was dominant accounting for 42% (21/50) of cases. This was characterized by spindly stroma, discrepancy between glands and stroma, glandular hyperplasia, formation of polyps and clusters of thick walled vessels. (Figure 3). Anovulatory cycle accounted for 24% (12/50) cases. There were inactive or weakly proliferative glands in stroma showing numerous thin walled, telengiectatic vessels having fibrin thrombi and stromal breakdown. (Figure 4). An equivalent number of cases of chronic endometritis were seen (Figure 5) This was followed by pill effect endometrium seen in 6% (Figure 6) cases and a single case of atrophic endometrium (2%). The distribution of cases in different age groups and according to presenting complaints is given in Table II. Correlations of Age to diagnosis and Presenting complaints to diagnosis are given in Tables III and IV.

Table I: Distribution of Endometrial Pathologies

Diagnosis	Number of Cases
Estrogen dominance endometrium	21
Anovulatory	12
Chronic endometritis	12
Pill effect endometrium	3
Atrophic endometrium	1
Endometrial carcinoma	1
Total	50

Figure 1: Distribution of Benign and Malignant Lesions of the Endometrium



**P=0.000 There is a significant difference between the benign and malignant lesions*

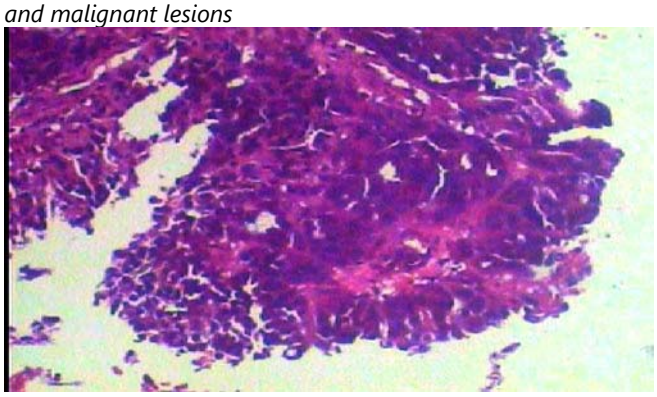


Fig 2: Endometrial carcinoma showing papillary formation and cytologic atypia (H&E (X100)

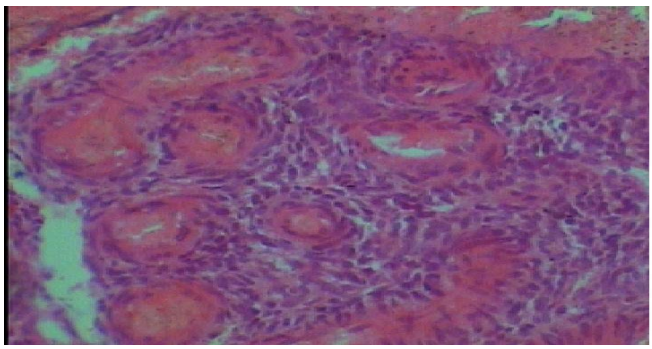


Fig 3: Estrogen Dominance Pattern; Cluster of thickened vessels and spindly stroma (H&E X 400)

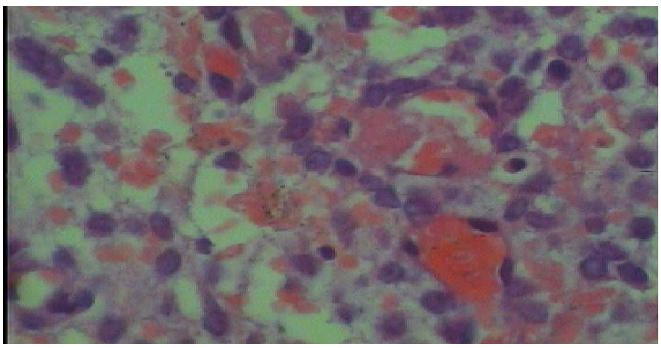


Fig 4: Anovulatory endometrium showing thin walled vessels with fibrin thrombi (H&E X 400)

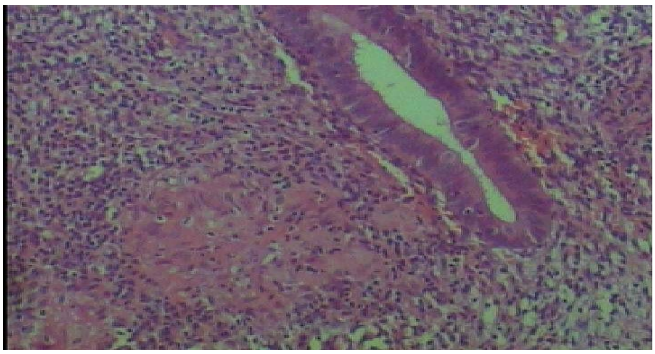


Fig 5: Chronic granulomatous inflammation showing epitheloid cell granuloma (H&E low power view x100)

Discussion

Endometrium is a dynamic, hormonally sensitive and responsive tissue which constantly and rhythmically undergoes changes in the active reproductive life. The pathological changes can be easily evaluated by microscopy.[7] Dysfunctional Uterine Bleeding is very commonly observed in clinical practice. The endometrium is a sensitive bioassay for estrogen and progesterone whose actions are mediated by acting on specific receptors.[8]

In ovulatory cycles it is shed in a cyclic, predictable fashion. The adequate synthesis of progesterone receptors in the endometrial epithelial cells by the estrogen in the follicular phase is essential for the formation of secretory endometrium, so that progesterone alone without the estrogen priming effect will not cause endometrial bleeding when its levels decline.

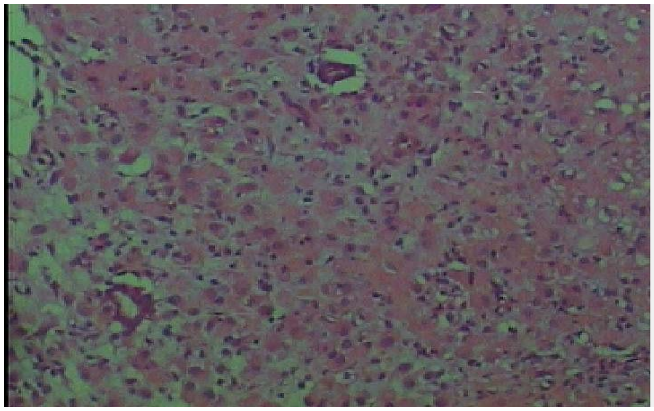


Fig 6: Pill effect endometrium showing small, inactive glands and decidulized stroma (H&E 200)

Without ovulation and subsequent progesterone production, a state of "unopposed" continuous estrogen secretion occurs. This stimulates excessive dilation of the spiral arterial supply and abnormal endometrial growth without adequate stromal support. The endometrium outgrows its blood supply. The consequence is spontaneous breakage and sloughing of the endometrium with unpredictable bleeding. Close to menopause there is aberrant follicular recruitment, decreased level of estradiol and shortened proliferative phase.

Fluctuating estrogen levels results in irregular bleeding and eventually ovulation completely stops. Therefore in anovulatory cycles, the estrogen levels can either be high as in hyperplasia or low as in atrophic endometrium.[9]

Table- II: Distribution of cases in different Age groups

Age group	Diagnosis	Number of cases	Percentage
20-30 years	Estrogen dominance	2	28.8
	Anovulatory	1	14
	Chronic Endometritis	3	42
	Pill effect	1	14
	Total	7	100
31-40 years	Estrogen dominance	7	58.3
	Anovulatory	1	8.3
	Chronic Endometritis	4	33.3
	Total	12	100
41-50 years	Estrogen dominance	12	44.4
	Anovulatory	8	29.6
	Chronic Endometritis	5	18.5
	Pill effect	2	7.4
	Total	22	100
51-60 years	Anovulatory	2	100
61-70 years	Atrophic	1	50
	Endometrial carcinoma	1	50
	Total	2	100

Table III: Age versus Diagnosis

Diagnosis	<40 years	>40 years	Total
Estrogen dominance	7	14	21
Anovulatory	2	10	12
Chronic Endometritis	5	7	12
Endometrial Carcinoma		1	1
Others	1	3	4

Table- IV: Presenting complaint versus diagnosis

Diagnosis	Cyclic	Acyclic	Total
Estrogen dominance	15	6	21

Anovulatory	8	4	12
Chronic Endometritis	9	3	12
Endometrial Carcinoma		1	1
Others	3	1	4
Total	35	15	50

Although the withdrawal or decline of both estrogen and progesterone results in sloughing of the endometrium but the mechanisms are different. The progesterone withdrawal causes spasmodic constriction of the spiral arterioles, which become prominent under its effect, followed by ischemia and desquamation of the endometrium. The marked increase in the PGF2α by progesterone in the luteal phase seems to be responsible for it. PGF2α is a potent vasoconstrictor while PGE2 is a vasodilator. The critical ratio of PGF2α and PGE2 is responsible for vasoconstriction of spiral arterioles of the endometrium. In anovulatory uterine bleeding only estrogen is present, progesterone being absent.[10] The pattern of bleeding in anovulatory cycle thus depends entirely on the duration and level of estrogen stimulation on the endometrium. In the absence of progesterone, the markedly decreased ratio of PGF2a to PGE2 may account for the nature of uncontrolled bleeding seen in these conditions.[9,10] Sometimes, in evident ovulation, abnormal uterine bleeding occurs, because of disturbance in the delicate estrogen progesterone balance responsible for maintaining endometrial integrity. The blood vessels start to develop in late proliferative phase and continue to do so in luteal phase and become especially prominent on day twenty three of the menstrual cycle when they are surrounded by predecidua.[7,8] At time of menstruation these vessels contract and then relax resulting in seepage of blood. The vessels of functional layer lack elastin and cannot stay contracted for long. They are shed with the functionalis and fail, therefore, to contribute to uterine hemostasis. The hemostasis is brought about by constriction of basal arteries in denuded basal layer and radial and arcuate arteries in the myometrium. But when there is hormonal imbalance i.e. estrogen is relatively higher than progesterone the vessels do become thick and form clusters, but the surrounding stroma remains spindly and no decidual changes are present. Such endometria may remain flat or form pseudopolyps.[8,11] These vessels are not totally sloughed at the time of menstruation as in normal cycle. The remaining sprouts continue to persist in the next cycle and as they are not easily blocked so increased bleeding occurs.[12] We termed such hormonal imbalance as Estrogen Dominance Pattern of endometrium (EDP).When long standing it can lead to various types of hyperplasias.[8] If hormonal imbalance is such that progesterone is completely absent then the vessels fail to develop and under the constant estrogen influence they remain thin and telengiectatic. Such vessels are easily thrombosed and there is continous seepage of blood into the stroma. This condition is commonly known as hemorrhagic or anovulatory endometrium.[7,8,,13]

In 50 cases we studied five patterns of endometrial abnormalities were observed among the benign cases. The most frequent observation in almost all age groups was related to high estrogenic sate termed as Estrogen Dominance Pattern of endometrium, this is similar to the findings of Vakiani et al.[14] in about 1300 cases. They concluded that dysfunctional abnormal uterine bleeding was found more often at the climacteric and chiefly in the form of anovulatory endometrium.

In our cases of hyperplasia only simple typical hyperplasia was noted. . This is similar to a study from Italy by Garuti et al which showed 51% cases of simple hyperplasia, 15% cases of complex hyperplasia and 7.7% cases of atypical hyperplasia, thus making simple hyperplasia the most common type.[10]

Anovulatory cycles was the second most frequent diagnosis in our study. 8/12 (66.6%) cases of anovulatory endometrium were in age group 41-50 years. This is in accordance with the observation made by Kailas who explains perimenopause as the transition from normal ovulation to anovulation which then eventually leads to permanent loss of ovarian function[15] Farquhar et al in their study of 1033 cases had 46 cases of hyperplasia and 5 of carcinoma. The risk factors for endometrial hyperplasia in premenopausal women with abnormal menstrual bleeding were body weight >/=90 kg, age >/=45 years, infertility, family history of colonic carcinoma, and nulliparity.[13] According to Phutkarzade and Chomakhashvili endometrial hyperplasia is associated with shortened and prolonged persistence of ovarian follicles and it is not a separate nosological phenomenon and effectiveness of its treatment strongly depends on the condition of ovary and hormone systems.[16] Bender has recommended

the use of hysteroscopy along with dilatation and curettage in evaluation of perimenopausal bleeding.[17] In a study from Karachi on 328 patients with postmenopausal bleeding showed hyperplasia and atrophic endometrium as common causes of bleeding. Endometrial carcinoma was present in 10.6% of their cases.[18] In our study the patient (20% of patients with postmenopausal bleeding) with endometrial adenocarcinoma was 65 years old and had been menopausal for last 13 years and had presented with repeated episodes of bleeding over the past two weeks. Iatrikis et al have also shown that repeated episodes of postmenopausal bleeding are most probably associated with carcinoma.[19]

In our study there were 24% (12/50) cases of chronic endometritis. Two of which were diagnosed as chronic granulomatous inflammation. The diagnosis of chronic endometritis is made on the basis of presence of plasma cells. The morphologic features found to be of value in diagnosing this condition are superficial stromal edema, spindly stroma, difficult to date endometrium and stromal inflammatory infiltrate dominated by lymphocytes in the absence of premenstrual changes or any other significant pathologic endometrial lesions. Greenwood and Moran claim that when these changes are present, a plasma cell infiltrate is invariably found.[20,] Immunohistochemical stains can help in detecting plasma cells. Crum has used immunoperoxidase[21], Bayer used Syndecan –1[22], Yorukoglu has used methyl green pyronin for this purpose and claims that it helps in distinguishing the stromal cells from plasma cells.[23] A study from India showed 2.6% cases of infertility were due to tuberculous endometritis.[24] A study from Rawalpindi showed 10% out of 50 infertile patients as having tuberculous endometritis.[25]

Conclusion

Our study on endometrial curetting histopatholgy in abnormal uterine bleeding revealed that most cases are clustered around the perimenopausal age. Our study showed that there was relative estrogen excess termed as Estrogen Dominance Pattern (EDP) over progesterone leading to specific changes such as clusters of thickened blood vessels, spindly stroma, weak or absent secretory changes in the glands and stroma with or without polyp formation. We also noted frequent anovulatory pattern in the older age.

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